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| 10/074,225 | 02/14/2002 | Fernando Donate | 38342-178463 | 6196 |

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| EXAMINER | |
|---|---|
| BLANCHARD, DAVID J | |

| ART UNIT | PAPER NUMBER |
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| 1643 | |

DATE MAILED: 07/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/074,225 | DONATE ET AL. | |
| | Examiner | Art Unit | |
| | David J. Blanchard | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *18 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5 and 7-57* is/are pending in the application.

4a) Of the above claim(s) *3,4,16-48 and 50-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 5, 7-15, 49 and 56-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 1-5 and 7-57 are pending.

Claims 1-5, 7, 11-13 and 49 have been amended.

Claims 52-57 have been added.

Claims 3-4, 16-48 and 50-55 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

2. Claims 1-2, 5, 7-15, 49 and 56-57 are under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This Office Action contains New Grounds of Rejections.

### *Election/Restrictions*

5. Applicant's response at page 11 states that the Office and Applicant apparently overlooked the fact that claim 2 should have been included with Group 1, since group 2 is a subgenus of claim 1(d) that selects three of the four possible sequences of SEQ ID NO:7. Applicant is reminded that claim 2 was part of Group 3 of the restriction requirement mailed 7/28/2004 and was properly restricted for reasons set forth therein. Applicant did not traverse the restriction requirement with respect to the invention of Group 3 and thus, claims 1-2, 5-15 and 49 as they pertain to the pentapeptide of SEQ ID NO:7 and the three species inclusive therein (i.e., SEQ ID NOS:8-10) were not examined in the previous Office Action mailed 11/17/2004. This should also clarify applicant's misunderstanding of the objection to claim 1 as being drawn to non-elected

subject matter (Applicant response at bottom of page 11) (see also item no. 3 of the Office Action mailed 11/17/2004).

During the telephonic interview conducted on 15 April 2005, applicant pointed out that claim 2, a subgenus of claim 1(d) is encompassed by a search of SEQ ID NO:5 and SEQ ID NO:6 as these peptides comprise the pentapeptide of SEQ ID NO:7 (i.e., H/P domain). Since the pentapeptides of SEQ ID NO:7 are encompassed by a search of the human and rabbit HPRG sequences (i.e., SEQ ID NOS:5 and 6), the restriction requirement between Groups 1-3 is hereby withdrawn.

With respect to claims 3-4, claims 3-4 are drawn to chemical structures and sequences that are distinct from the sequences of groups 1-3 and require further search and consideration. Thus, claims 3-4 and newly added dependent claims 52-54 will not be rejoined at this time.

For clarity of the record it is reiterated that the restriction requirement between the inventions of Groups 1-3 of the restriction requirement mailed 7/28/2004 is hereby withdrawn. Restriction between all other groups as set forth in the restriction requirement mailed 7/28/2004 is deemed to be proper and made FINAL.

***Objections/Rejections Withdrawn***

6. The objections to claims 1, 5-7, 11-12 and 49 as being drawn to non-elected inventions is withdrawn in view of the amendments to the claims.

7. The rejections of claims 1, 5, 7-15 and 49 under 35 U.S.C. 112, second paragraph, for indefiniteness are withdrawn in view of the amendments to the claims.

8. The rejection of claims 1, 5-15 and 49 under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement is withdrawn in view of applicant's arguments and amendments to the claims.

9. The rejection of claims 1, 5-15 and 49 under 35 U.S.C. 112, first paragraph for lack of enablement is withdrawn in view of applicant's arguments and the amendments to the claims.

10. The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Koide et al is withdrawn in view of the amendments to the claim.

11. The rejection of claims 1, 11, 13 and 49 under 35 U.S.C 102(b) as anticipated by Borza et al is withdrawn in view of the amendments to the claims.

12. The rejection of claims 1, 5-15 and 49 under 35 U.S.C. 102(e) as anticipated by Simantov et al is withdrawn in view of the amendments to the claims.

***Response to Arguments***

13. The rejection of claims 1, 5-15, 49 and applied to newly added claims 56-57 under 35 U.S.C. 102(e) as being anticipated by Olsson et al as evidenced by Koide et al and Borza et al is maintained.

The response filed 4/18/2005 has been carefully considered, but is deemed not to be persuasive. The response states that the amendments to the claims distinguishes them from the teachings of Olssen et al. Further, applicant submits a Rule 131 declaration of co-inventor Fernando Donate showing notebook pages that support a date of invention prior to the earliest priority date of the published Olssen patent

application 05 February 2005. In response to these arguments, Olssen et al teach fragments of the human and rabbit HPRG polypeptides which include, but are not limited to the H/P domain (i.e., SEQ ID NO:5 and SEQ ID NO:6), and which polypeptides are not the full-length human or rabbit HPRG (see pages 1, 3 (right column), and page 4 at paragraph [0042]). Thus, Olsson et al as evidenced by Koide et al and Borza et al still reads on the claims. The Declaration filed on 4/18/2005 under 37 CFR 1.131 has been considered but is ineffective to overcome the Olssen et al reference. The evidence submitted is insufficient to establish conception of the invention prior to the effective date of the Olssen et al reference. While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897). The evidence submitted is insufficient to establish conception of presently claimed functionally equivalent variants of the human and rabbit H/P domain of HPRG, which comprise conservative amino acid substitutions. There is no evidence of conception of any such molecules as defined by the claims. Further, the evidence submitted is insufficient to establish a reduction to practice of the invention in this country or a NAFTA or WTO member country prior to the effective date of the Olssen et al reference because the present claims encompass conservative amino acid substitution variants of the H/P domain of human and rabbit HPRG having substantially the same ligand binding activity or other functional activity (i.e., inhibiting

angiogenesis). The declaration does not provide sufficient evidence that the claimed functional variants of the human and rabbit H/P domains had been diligently reduced to practice. See MPEP 715.07.

Additionally, the declaration is not signed by all of the inventors and applicant has not shown that less than all of the named inventors of the instant application invented the subject matter of the claims under rejection (see MPEP 715.04). Applicant is reminded that the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

For these reasons the rejection is maintained.

***New Grounds of Rejections***

14. Claim 57 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form. Claim 57 depends from claim 56, which recites that the human H/P domain which includes the consensus sequence of SEQ ID NO:7 and consists essentially of residues 350 to 408 in human HPRG (SEQ ID NO:1), however, claim 57 recites a fragment of the human H/P domain that has residues 380 to 408 of SEQ ID NO:1. Because claim 57 does not include every limitation of the claim on which it reads (i.e., does not include residues 350-379 of human HPRG), claim 57 does not further limit claim 56 from which it depends.

15. Claims 1-2, 5, 7-15, 49 and 56-57 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention.

The claims are indefinite in the recitation of "human HGRP" and "rabbit HGRP" in the last two lines of claim 1. The acronym is not defined by the claims or the specification and it is unclear whether the "human HGRP" and "rabbit HGRP" polypeptides are the same polypeptides that comprise the human and rabbit HPRG polypeptides comprising the claimed H/P. Did applicant intend "HGRP" to be HPRG?.

16. Claims 1-2, 5, 7-15, 49 and 56-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

The response filed 4/18/2005 has introduced NEW MATTER into the claims. The claims have been amended with the proviso that the anti-angiogenic polypeptide or peptide of the present claims is not the full-length human HPRG as defined by SEQ ID NO:1 or full-length rabbit HPRG as defined by SEQ ID NO:3. The response states that the present amendments do not introduce any new matter, however, the response did not point out where support for the presently amended claims could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting

evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 ("Applicant should therefore specifically point out the support for any amendments made to the disclosure."). After review of the disclosure as-filed, the disclosure does not provide adequate written support for the negative proviso of claim 1 that the claimed polypeptide or peptide is not the full-length human or rabbit HPRG polypeptide. While the specification generally discloses fragments of the human and rabbit HPRG polypeptides, including the H/P domains of said polypeptides, where is it contemplated that the presently claimed polypeptides or peptides exclude the full-length human and rabbit HPRG polypeptides? There is no express or inherent written support for the exclusionary provision of the presently claimed polypeptides or peptides. Further, there is inadequate written support for the anti-angiogenic polypeptides comprising the H/P domain of human or rabbit HPRG that are not the full-length human or rabbit HPRG wherein the polypeptides bind just any ligand. The disclosure does not adequately support the correlation between the anti-angiogenic properties of the presently claimed polypeptides or variants and the binding to just any ligand as broadly as is claimed. As presently amended claims 1-2, 5, 7-15 and 49 now recite limitation, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in presently amended claims 1-2, 5, 7-15 and 49, which did not appear in the specification, as-filed, introduce new concepts and violate the description requirement of the first paragraph of

35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in presently amended claims 1-2, 5, 7-15 and 49 in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

With respect to newly added claims 56-57, the response indicated that support for these claims could be found at page 16, line 26, where it is stated that "a preferred peptide comprises a minimal consensus sequence [H/P][H/P]PHG (SEQ ID NO:7) and in the disclosure elsewhere of multimers of the consensus sequence. In response, claims 56-57 are drawn to N-terminal fragments of the human and rabbit H/P domain, which includes the consensus sequence of SEQ ID NO:7 and consists essentially of residues numbered as residues 350 to 408 in human HPRG (SEQ ID NO:1) or consists essentially of residues numbered as residues 328 to 405 in rabbit HPRG (SEQ ID NO:3). The specification at page 16, line 26 does not support the claimed polypeptides or peptides, which are N-terminal fragments of the human H/P domain that consist essentially of residues 350 to 408 in human HPRG or N-terminal fragments of the rabbit H/P domain that consists essentially of residues 328 to 405 in rabbit HPRG or in the case of newly added claim 57 has the sequence of residues 380 to 408 of human HPRG. The disclosure of a consensus sequence found in the H/P domain of HPRG polypeptides does not provide adequate written support for the narrower limitations of the present claims, which are drawn to N-terminal fragments of the H/P domains and comprise specifically identified residues. Further, there is inadequate written support for the claimed anti-angiogenic polypeptides comprising an N-terminal fragment of the H/P

domain of human or rabbit HPRG that are not the full-length human or rabbit HPRG wherein the polypeptides bind just any ligand. The disclosure does not adequately support the correlation between the anti-angiogenic properties of the presently claimed polypeptides or variants and the binding to just any ligand as broadly as is claimed. Such limitations recited in newly added claims 56-57, which did not appear in the specification, as-filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in newly added claims 56-57 in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

17. Claims 1-2, 11, 13 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Borza et al (Biochemistry, 35:1925-1934, 1996, Ids reference #2, filed 6/6/02) as evidenced by Donate et al (Cancer Research, 64(16):5812-5817, 15 August 2004).

The claims are drawn to anti-angiogenic polypeptide or peptide having the sequence of the histidine-proline rich (H/P) domain of human histidine-proline rich glycoprotein (HPRG) (SEQ ID NO:5) or the H/P domain of rabbit HPRG (i.e., SEQ ID NO:6) or conservative amino acid substitution variants of SEQ ID NOS:5 or 6 or a pentapeptide consensus sequence from said H/P domain having the sequence (His/Pro)-(His/Pro)-Pro-His-Gly (SEQ ID NO:7) or addition variant thereof having an additional 1 to 4 amino acids selected from His, Pro or Gly at the N- or C-terminus of the

pentapeptide, wherein the polypeptide is not human HPRG (SEQ ID NO:1) or rabbit HPRG (SEQ ID NO:3) (i.e., not the full-length HPRG). Further, the claims are drawn to an anti-angiogenic pharmaceutical composition comprising the H/P domain of the human or rabbit HPRG polypeptide or the pentapeptide of SEQ ID NO:7 and a pharmaceutically acceptable carrier and said pharmaceutical composition is in a form suitable for injection and an affinity ligand useful for binding to or isolating an HPRG-binding molecule comprising the polypeptide or peptide of claim 1 or 2 immobilized on a solid support or carrier. Applicant is reminded that the term "having" is interpreted as equivalent to "comprising", which is open-ended claim language and is inclusive to unrecited elements (MPEP 2111.03).

Borza et al teach the H/P domain from human and rabbit HPRG as well as the pentapeptide having the consensus sequence (His/Pro)-(His/Pro)-Pro-His-Gly (see entire document, particularly Figs 2-4, Table 1 and page 1927, right column). As evidenced by Juarez et al, the HHPHG pentapeptide domain binds to tropomyosin and inhibits angiogenesis and tumor growth in vivo and multimerization of the HHPHG exponentially increases its affinity for tropomysin, with a concurrent increase in antiangiogenic activity (see abstract). Thus, as a property is inherent to a product, the antiangiogenic activity of the H/P domain is necessarily present in the human and rabbit H/P domains taught by Borza et al. For example, in Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999); the following was noted. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a

scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. Thus, the H/P domain of human and rabbit HPRG as taught by Borza et al is a polypeptide "having" the sequence of the H/P domain of human and rabbit HPRG that is not the full-length human HPRG or rabbit HPRG.

Borza et al also teach the H/P domain of rabbit HPRG in 5 mM phosphate buffer, pH 7.2, which is reasonably interpreted to be a pharmaceutically acceptable carrier and in suitable form for injection (see page 1926, right column). For this rejection the intended use as an anti-angiogenic pharmaceutical composition is given no patentable weight. See MPEP 2111.02. Further, Borza et al teach the H/P domain of rabbit HPRG bound to a DEAE-cellulose column (i.e., solid support), which is interpreted as an affinity ligand useful for binding to or isolating an HPRG-binding molecule (see bridging paragraph of pages 1928-1929). Thus, Borza et al as evidenced by Donate et al anticipate the claims.

## *Claim Rejections - 35 USC § 103*

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 1-2, 5, 7-15 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borza et al (Biochemistry, 35:1925-1934, 1996, Ids reference #2, filed 6/6/02) in view of Azizkhan et al (Journal of Experimental Medicine, 152(4):931-944, 1 October 1980) and Simantov et al (US 2001/0041670 A1, 12/6/1999, cited previously on PTO-892 mailed 11/17/2004).

Claims 1-2, 11, 13 and 49 have been described supra. Claims 5, 7-10, 12 and 14-15 are drawn to a diagnostically and therapeutically labeled anti-angiogenic polypeptide or peptide comprising the H/P domain of the human or rabbit HPRG polypeptide (SEQ ID Nos:5 or 6, respectively) or the pentapeptide of SEQ ID NO:7, and a diagnostically acceptable carrier and a therapeutic anti-angiogenic pharmaceutical composition comprising said H/P domain of the human or rabbit HPRG polypeptide or

the pentapeptide of SEQ ID NO:7, which is bound to a therapeutically active moiety and a pharmaceutically acceptable carrier. Applicant is reminded that the term "having" is equivalent to "comprising", which is open-ended claim language and is inclusive to unrecited elements (MPEP 2111.03).

Borza et al have been described supra. Borza et al do not teach diagnostically or therapeutically labeled H/P domain of human or rabbit HPRG and a diagnostically or pharmaceutically acceptable carrier in suitable form for injection and wherein the label is selected from the labels recited in claims 8-10 and 15. These deficiencies are made up for in the teachings of Azizkhan et al and Simantov et al.

Azizkhan et al teach that heparin secreted by mast cells stimulates capillary endothelial cell migration, which is an important component of angiogenesis in vivo and the migratory activity of heparin was blocked by heparin specific antagonists (see entire document, particularly abstract).

Simantov et al teach pharmaceutical compositions comprising an HPRG polypeptide and a pharmaceutically acceptable carrier (also interpreted as a diagnostically acceptable carrier) (see page 3, paragraphs [0039-0040] and page 6 paragraph [0084]) and Simantov et al teach various diagnostic and therapeutic labels including radionuclides, fluorescein, rhodamine, Texas red and phycoerythrin as well as others (see page 10 and page 13, paragraph [0174]).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced compositions comprising diagnostically or therapeutically labeled human or rabbit H/P domains of HPRG taught

by Borza et al to block heparin stimulated capillary endothelial cell migration (i.e., angiogenesis) in view of the teachings of Azizkhan et al and Simantov et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced compositions comprising diagnostically or therapeutically labeled human or rabbit H/P domains of HPRG taught by Borza et al to block heparin stimulated capillary endothelial cell migration (i.e., angiogenesis) in view of the teachings of Azizkhan et al and Simantov et al because Borza et al teach the H/P domain of human and rabbit HPRG, which binds heparin (see pages 1931 and 1933, left columns) and Azizkhan et al teach that heparin secreted by mast cells stimulates capillary endothelial cell migration, which is an important component of angiogenesis in vivo and the migratory activity of heparin was blocked by heparin specific antagonists and Simantov et al teach pharmaceutical compositions comprising an HPRG polypeptide or fragment thereof and a pharmaceutically/diagnostically acceptable carrier and Simantov et al teach various diagnostic and therapeutic labels including radionuclides, fluorescein, rhodamine, Texas red and phycoerythrin as well as others for labeling the HPRG polypeptide or fragment thereof. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have diagnostically or therapeutically labeled the H/P domains of Borza et al with the diagnostic and therapeutic labels taught by Simantov et al to detect secreted heparin as an angiogenesis marker or to block the migratory activity of heparin and hence, angiogenesis or migration of capillary endothelial cells. Further, one of ordinary skill in the art would have been motivated to

combine the diagnostically/therapeutically labeled H/P domain of human or rabbit HPRG with a pharmaceutically acceptable carrier to facilitate therapeutic administration of the labeled polypeptides. Thus, it would have been obvious to one skilled in the art at the time the invention was made to have produced compositions comprising diagnostically or therapeutically labeled human or rabbit H/P domains of HPRG taught by Borza et al to block heparin stimulated capillary endothelial cell migration (i.e., angiogenesis) in view of the teachings of Azizkhan et al and Simantov et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

## ***Conclusion***

20. No claim is allowed.

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D
PRIMARY EXAMINER